15. (New) The method of claim 4 wherein the pathogenic microorganism is *Listeria monocytogenes*.

16. (New) The method of claim 4 wherein the protease is a metalloprotease.

REMARKS

Claim Amendments

Support for amended Claims 1-4, 8, and 9 and new Claims 10-16 are found throughout the specification, for example, at page 4, lines 16-24, page 6, lines 6-18, page 8, line 27 to page 11, line 24, and in the claims as originally filed. No new matter is added by these amendments.

Restriction Requirement

Responsive to the Restriction requirement, the claims of Group I (Claims 1-2) drawn to methods of detecting the presence or absence of a prokaryotic micriorganism are elected for prosecution. Applicant reserves the right to file a continuing application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicant does not hereby abandon or waive any rights in the non-elected inventions.

The requirement is being traversed for the reasons set forth in detail below.

The Examiner has issued a Restriction Requirement setting forth the following six groups: Group I (Claims 1-3); Group II (Claim 4); Group III (Claim 5); Group IV (Claims 6-7); Group 5 (Claim 8); and Group VI (Claim 9). The Examiner states that restriction is proper because (1) the inventions of Groups I-III and VI are drawn to distinct methods, which differ in method objectives, method steps and materials used; and (2) the inventions of Groups IV and V are drawn to two different specifically, technically, and mechanically distinct products. In

addition, the Examiner states that the inventions of Groups II and V are related as process and apparatus for its practice, but are distinct because the process as claimed can be practiced by another materially different apparatus or by hand. Applicant respectfully traverses.

The inventions of Groups I and II are interrelated. Firstly, the methods relate to determining the presence of microorganisms in a sample by identifying a protease that is unique to the microorganism; providing a quenched labeled broad spectrum substrate for the protease; providing the sample; and determining the presence of absence of a detectable label, which indicates the presence of absence of the microorganism. Thus, the inventions of Groups I and II employ the same methods. In addition, the invention of Group I includes embodiments which are also embraced by the invention of Group II. The microorganisms to be detected by the invention of Group I are prokaryotic microorganisms, and the microorganisms to be detected by the invention of Group II are pathogenic microorganisms. In particular, determining the presence of the prokaryotic microorganisms of the invention of Group I embraces determining the presence of the pathogenic organisms of the invention of Group II, and *vice versa*. As such, the restriction requirement between Groups I and II is improper.

In addition, Applicant submits that the examination of Groups I and II together would not place an undue burden upon the Examiner. A search of the prior art for the invention of one group would also identify prior art that is applicable to the other group. Furthermore, in light of the close relationship of the invention of Group I, a complete search of one invention would entail a search of the invention of Group II. For example, a search of prior art for the methods defined by Group I would identify prior art that is applicable to Group II. As such, Applicant submits that no excessive searching burden would be placed upon the Patent Office in examining Groups I and II together.

For the foregoing reasons, withdrawal of the restriction requirement is respectfully requested.

Applicant has amended claims 1-4, 8, and 9, and added Claims 10-16 herein. Applicant submits that Claims 1-3, and 10-12 correspond to Group I of the Restriction Requirement, as they

recite methods for detecting the presence or absence of a prokaryotic microorganism in a sample. Applicant also submits that Claims 4, and 13-16 correspond to Group II of the Restriction Requirement as they recite methods for detecting pathogenic microorganisms in a sample. Applicant respectfully requests entry of the claim amendments and further examination of Claims 1-4 and 10-16.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Karen J. Townsend

Karen J. Townsend
Registration No. 50,675
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Dated: February 3, 2003

MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

1. (Amended) A method for detecting the presence or absence of a prokaryotic microorganism in a sample, the method comprising the steps of:

[a. identifying a protease that is unique to the prokaryotic microorganism;

b. providing a quenched labeled substrate specific for said protease; and

c. providing the sample; and

d. determining the presence or absence of a detectable label.]

a) contacting a test sample with a substrate specific for a protease that is unique to a prokaryotic microorganism; and

b) detecting cleavage of the substrate or absence of cleavage of the substrate, wherein cleavage of the substrate is indicative of the presence of the prokaryotic microorganism in the sample, and absence of cleavage of the substrate is indicative of the absence of the prokaryotic microorganism in the sample.

2. (Amended) The method of claim [1] 10 wherein the quenched label is selected from the group consisting of fluorescent [labeled peptide] label and a colorimetric [labeled] label [peptide].

3. (Amended) The method of claim 2 wherein [the means for determining is] the cleavage is detected using a colorimeter or fluorimeter.

4. (Amended) A method for detecting a plurality of pathogenic microorganisms in a sample, the method comprising the steps of:

[a. identifying a protease that is unique to the [prokaryotic] pathogenic microorganism;

b. providing a quenched labeled broad spectrum substrate for said protease;

c. providing the sample; and

d. determining the presence or absence of a detectable label.]

a) contacting a test sample with a substrate specific for a protease that is unique to a pathogenic microorganism; and

b) detecting cleavage of the substrate or absence of cleavage of the substrate, wherein cleavage of the substrate is indicative of the presence of the pathogenic microorganism in the sample, and absence of cleavage of the substrate is indicative of the absence of the pathogenic microorganism in the sample.

8. (Amended) A sensor for detection of [bacteria] a microbial pathogen in a sample, said [device] sensor comprising packaging material having a first side proximal to said sample and having a second side; and [a dye labeled substrate for the bacteria wherein said dye labeled substrate is] having a detectably labeled substrate specific for a protease produced by said microbial pathogen attached to said first side.

9. (Amended) A method for using an alpha-crystallin type protein comprising the steps of:

[(a)] a) expressing and purifying the recombinant alpha-crystallin type protein; and

[(b)] b) adding the alpha-crystallin type protein to a solid phase or a liquid phase assay containing a day labeled peptide in an amount sufficient to reduce proteolysis of said dye labeled peptide.